Providence St. Joseph's and St. Michael's Healthcare ("Network")
Guidelines for Reporting Protocol Deviations to the
Research Ethics Board (REB)
June 07, 2018

1. Introduction

The purpose of this guidance document is to provide researchers with information on the handling and reporting of protocol deviations. The Providence St. Joseph's and St. Michael's Healthcare (Network) Research Ethics Board (REB) requires investigators to submit information regarding a protocol deviation, in general, that had not received prior approval by the REB, because the deviation was necessary to ensure research participant safety, was of an inadvertent nature, or was a minor administrative or logistical change (i.e., change in monitor(s), change in contact numbers). Investigators are required to report only protocol deviation(s) that involve research participants or procedures under the jurisdiction of the Network REB.

2. Definition of a Protocol Deviation

Protocol Deviation: an unanticipated or unintentional divergence or departure from the expected conduct of an approved study that is not consistent with the current approved research protocol, consent document or study addenda. Deviations may or may not have a significant effect on the research participant's rights, safety or welfare, or on the integrity of the data. Deviations are different from amendments in that they generally apply to a single occurrence or participant and are not intended at the time to modify the entire protocol.

Note: The term **'protocol deviation'** and **'protocol violation'** may be used interchangeably.

3. ICH Good Clinical Practice (GCP) Requirements

The following ICH Good Clinical Practice (GCP) guidelines can be applied to all REB approved research studies.

ICH GCP (Article 4.5.2) states:
"The investigator should not implement any deviation from, or changes of the protocol without agreement by the sponsor and prior review and documented approval/favourable opinion from the [REB] of an amendment, except where necessary to eliminate an immediate hazard(s) to trial subjects, or when the change(s) involves only logistical or administrative aspects of the trial (e.g. change in monitor(s), change in telephone number(s))."

ICH GCP (Article 4.5.4) also states:
"The investigator may implement a deviation from, or a change of, the protocol to eliminate an immediate hazard(s) to [research participants] without prior [REB] approval/favourable opinion. As soon as possible, the implemented deviation or change, the reasons for it, and, if appropriate, the proposed protocol amendment(s) should be submitted:

(a) to the [REB] for review and approval/favourable opinion
(b) to the sponsor for agreement, [if required]
(c) to the regulatory authority(ies), if required"

The investigator or designee is required to document and explain all protocol deviations.
ICH GCP (Article 4.5.3) states:
"The investigator, or person designated by the investigator, should document and explain any deviation from the approved protocol."

4. What Protocol Deviations must be reported to the REB?

The following are types of protocol deviations that require reporting to the REB:

- change in study procedure(s) initiated to eliminate immediate hazards to research participants;
- enrolment of a research participant who did not meet all protocol inclusion/ exclusion criteria, whether agreed to or not by the study Sponsor;
- over-enrolment (exceeding the target number of participants approved by the REB);
- deviation in the consent process (i.e., failure to obtain informed consent, use of an invalid consent form, missing date of consent, missing signature);
- performance of a study procedure not approved by the REB;
- failure to perform a required study procedure that, in the opinion of the investigator, may affect participant safety **or** data integrity;
- study procedure (i.e., study visit) performed outside of the required timeframe that, in the opinion of the investigator, may affect participant safety **or** data integrity;
- study drug/intervention errors (i.e., incorrect study drug/intervention, incorrect dosage of the study drug);
- breach of confidentiality whereby a research participant's personal health information (PHI) is revealed to a person without a need to know, or by data exposure (i.e., digital device security breach, documents containing PHI are left unsecured).

See ***Section 7*** for examples of protocol deviations that **do not** require reporting to the REB.

5. How to Complete the Network REB Protocol Deviation Reporting Form

When a protocol deviation has occurred within a study and it meets the criteria for reporting to the REB, the investigator must complete and sign the REB Protocol Deviation Reporting Form. The report must also include the following information:

- The unique coded identifier of the research participant (do not include any personal health information);
- A description of the protocol deviation that occurred with a full explanation of the circumstances that lead to the deviation and the participant's outcome;
- A description of how the event was handled including what steps were taken or that will be taken to correct/address the problem resulting from the deviation;
- A plan for ensuring that a similar deviation does not occur in the future;
- The documentation of the contact with the study Sponsor (if applicable) regarding the deviation and outcome;
- An explanation of how the deviation did/did not increase the risk or the possibility of risk for the research participant(s);

- An explanation of how the deviation did/did not compromise the scientific integrity of the entire study;
- A description of any planned changes to the study protocol and/or consent documents.

6. Report Timing and Process

All Network reportable protocol deviations must be reported to the REB within **fifteen (15)** calendar days of the investigator becoming aware of the protocol deviation using the Network REB Protocol Deviation Reporting Form.

Two (2) copies of the form (1 copy for the REB and 1 copy for the investigator) should be submitted to the REB. Each protocol deviation report submitted to the REB will be acknowledged and reviewed by the REB. The REB may require further actions in follow-up of the protocol deviation.

Except in case of an emergency or change(s) to eliminate an immediate hazard to research participant(s), the investigator may be required to obtain prior documented approval from the study Sponsor for the protocol deviation or change in the study protocol, if applicable.

If the protocol deviation necessitates a change in the protocol and/or consent form or the protocol deviation is a minor logistical or administrative change to the study (e.g. change in study personnel contact numbers), the investigator should submit a study amendment to the REB using the Network REB Amendment and Administrative Change Request Form.

If the protocol deviation resulted in a serious adverse event (SAE) / unanticipated problem (unexpected, related or possibly related and involving greater risk of harm), the investigator should submit the SAE / unanticipated problem to the REB using the Network REB Local Serious Adverse Event / Unanticipated Problem Reporting Form.

If the protocol deviation impacts the rights, safety or well-being of research participants or the scientific integrity of the study protocol, the investigator may also be required to report the protocol deviation to local regulatory authorities, as applicable.

7. What Protocol Deviations do NOT require reporting to the REB?

Examples of minor deviations that do not usually require reporting to the REB include, but are not limited to:

- isolated cases of a study procedure, i.e. study visit, outside the required timeframe that does not create risk;
- isolated cases of missed required lab tests that does not create risk;
- isolated cases of missed/late study drug doses;
- lost medication diaries

If minor protocol deviations impact participant safety or data integrity of the entire study i.e., repeatedly missed key study tests or study outcome measures, this may require reporting to the REB.

All protocol deviations should be documented in the study files. The investigator is required to explain and sign off on all protocol deviations. This can be done using a Protocol Deviation Log. (See the REB website for a template of a Protocol Deviation Log.) The investigator must also report all protocol deviations to the study Sponsor, if applicable.

If required by the study Sponsor, the investigator may submit a copy of the study Protocol Deviation Log listing all protocol deviations to the REB with the annual Network REB Continuing Review Report.

REFERENCES

The International Conference on Harmonization (ICH) E6(R2): Good Clinical Practices (GCP) Section 4, 2016.

University of British Columbia (UBC) Clinical Research Ethics Boards: Guidance Note for Submitting Protocol Deviations to the REB, July 24, 2006.

IRB Services, General Guidance: Investigator Responsibilities, v10, April 15, 2013.

University of Manitoba Bannatyne Campus Research Ethics Boards: Submission Procedures for Submitting Protocol Deviations, January 20, 2007.